REMARKS

Interview Summary

Applicants thank Primary Examiner J.D. Schultz, Ph.D. for the telephone interview of January 4, 2006. During the telephone interview, Applicants discussed the Second Restriction Requirement and the Office's withdrawal of non-elected subject matter in the Office Action dated November 7, 2005. Applicants noted that the Second Restriction Requirement, dated September 7, 2005, partitioned each of the following RNA analogs into a separate group: peptide nucleic acids (Group I), ribozymes (Group II), and RNA aptamers (Group III). However, the Second Restriction did not place the "natural or synthetic RNA or of one or more coagulation-promoting fragments of natural or synthetic RNA," which are recited in claim 1, in a separate group. Applicants further noted that they contacted Examiner Bowman on October 5, 2005, who confirmed that the natural or synthetic RNA and fragments thereof were not part of the Restriction Requirement and would not be withdrawn as non-elected subject matter.

Applicants understanding of the Restriction Requirement is apparent in the Response to the Second Restriction Requirement, filed October 7, 2005. In the Response at page 3, Applicants "elected to prosecute Group 1, claims 1-3, drawn to a pharmaceutical preparation which comprises and amount, sufficient for promoting coagulation, of natural or synthetic RNA or of one or more coagulation-promoting fragments of natural or synthetic RNA or peptide-nucleic acids." Nonetheless, in the present Office Action, the Office withdrew non-elected subject matter from claim 1, which included the natural or synthetic RNA and fragments thereof. The Office stated

that "claim 1 is now being read as '[a] pharmaceutical preparation which comprises an amount, sufficient for promoting coagulation, of peptide-nucleic acids." Office Action at 3.

Because the Second Restriction Requirement failed to restrict natural or synthetic RNA and fragments thereof, and Examiner Bowman confirmed the same on October 5, 2005, Applicants assert that claim 1 should be read to include such subject matter as follows: "[a] pharmaceutical preparation which comprises an amount, sufficient for promoting coagulation, of natural or synthetic RNA, or of one or more coagulation-promoting fragments of natural or synthetic RNA, or peptide-nucleic acids."

Formal Matters

Applicants note that the Office did not consider foreign patent DE 199 03 693 A1, submitted in the Information Disclosure Statement filed August 1, 2003. The notation made by the Office next to the reference stated "no translation, not considered." In lieu of a translation, Applicants provided, as described in the Information Disclosure Statement itself, the English-language equivalent, U.S. Patent No. 6,528,299. Section 609.04(a) of the M.P.E.P. states that "[a]n English-language equivalent application may be submitted to fulfill this requirement if it is, in fact, a translation of a foreign language application being listed in an information disclosure statement. There is no requirement for the translation to be verified." Therefore, Applicants submit an additional copy of the Form 1449 and respectfully request that the Office indicate that it has considered DE 199 03 693 A1.

Applicants have amended claims 1 and 3. Applicants have canceled claim 2. Claims 1 and 2 are currently pending, with "ribozymes," "RNA analogs," and "RNA aptamers" withdrawn by the Office. Further, claims 4-12 have been withdrawn by the Office.

Enablement Rejection

The Office rejected claims 1-3, under 35 U.S.C. § 112, first paragraph, because the specification is not enabling. See Office Action at 4-8. Specifically, the Office Asserts that the specification is "enabling for promotion of coagulation *in vitro* using RNA as a procoagulant factor." Office Action at 4 (emphasis added). However, the specification allegedly "does not reasonably provide enablement for the treatment of a disease or disorder associated with coagulation via the administration of a pharmaceutical composition *in vivo*." Id. (emphasis added). Applicants respectfully traverse.

Applicants respectfully assert that the Office has mischaracterized the instant invention and that the assays described in the specification reasonably correlate to the claimed method, i.e. promoting coagulation. *See* M.P.E.P. § 2164.02. The instant invention is not directed to antisense therapy, or delivery of the PNA, natural, or synthetic RNA into the cell to inhibit gene expression, as the Office asserts. The following sections of the specification make this clear:

- "It has now been found, surprisingly, among the constituents released from injured tissues and cells the extracellular RNA represents an

important initial cofactor for the induction of . . . coagulation." Specification at 2, lines 37-39 (emphasis added).

- Extracellular RNA represents in this connection the natural "'foreign' surface for activating the plasma contact phase system." Specification at 3, lines 7-8 (emphasis added).
- "The realizations are supported by the observation that FSAP is able to bind specifically to RNA and is also redissociated by a hypertonic saline solution. It is thus remarkable that, under physiological conditions, specific binding only by RNA, and not by DNA, to FSAP is detectable." Specification at 3, lines 34-37.
- Examples 2-4 in the Specification describe the behavior of RNA in the plasma and the mechanism of RNA-dependent initiation of coagulation. *See* Specification at 9-10.

Thus, the instant invention does not suffer from the unpredictability of antisense oligomers passing through the cell membrane and inhibiting gene expression, as set forth in the references cited by the Office. Furthermore, Applicants respectfully assert that the assays, such as the turbidometric coagulation test, are recognized as correlating with the process of coagulation *in vivo*. Therefore, Applicants respectfully request that the Office withdraw the enablement rejection of claims 1-3.

Anticipation Rejections

The Office rejected claim 1 under 35 U.S.C. 102(b), as being anticipated by *Shimkets* (WO 00/58473) as evidenced by *Braasch* (Biochemistry, 41(14):4503-4510

(2002)). *See* Office Action at 8. In addition, the Office rejected claim 1 under 35 U.S.C. 102(b), as being anticipated by *Moore* (U.S. Patent No. 6,248,724) as evidenced by Braasch. *See* Office Action at 9. Specifically, the Office asserts that both *Shimkets* and *Moore* teach peptide nucleic acids (PNAs). Further, as evidenced by *Braasch*, "any PNA in high enough concentration would lead to toxicity, followed by cellular death and coagulation." Office Action at 8 and 9. Applicants respectfully traverse.

Applicants have amended claim 1, by adding "an activator for plasma coagulation factor" to the pharmaceutical preparation of claim 1. Applicants also canceled claim 2, which did not further limit the claims, as amended. As section 2131 of the M.P.E.P. states, "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Neither *Shimkets* nor *Moore* expressly mentions a pharmaceutical preparation containing an activator for plasma coagulation factor, as amended claim 1 recites. Further, the Office found that claim 2 was free of anticipatory prior art. Therefore, Applicants request that the Office withdraw the anticipation rejections of claim 1.

Obviousness Rejection

The Office rejected claims 1-3 under 35 U.S.C. §103(a), as being unpatentable over *Shimkets*, in view of *Kannemeier* (Eur. J. Biochem., 268:3789-3796 (2001)). *See* Office Action at 10. Specifically, the Office asserts that it would have been obvious to one of ordinary skill in the art to "incorporate the FSAP or FSAP proenzyme, as taught by Kannemeier et al. into the pharmaceutical composition comprising a PNA taught by Shimkets et al." Office Action at 11. Applicants respectfully traverse.

As set forth in M.P.E.P. § 2143.01, in order to establish a *prima facie* case of obviousness the Office must meet three criteria. "First, there must be some suggestion or incentive, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations." M.P.E.P. § 2143.01 and cases cited therein.

The Office has failed to establish a *prima facie* case of obviousness because there is no motivation to combine the references. The Office states that one would be motivated to combine the references because "the pharmaceutical composition of Shimkets et al. was designed to enhance coagulation, for example after trauma or hemophilia." Office Action at 11. However, the Office did not provide a citation within *Shimkets* for this statement. Contrary to the Office's assertion, *Shimkets* does not teach that the PNAs of the invention may be used to enhance coagulation. Applicants were only able to find a discussion of coagulation at page 89, lines 20-26 in reference to a "protein of the invention." Nowhere in *Shimkets* is there a suggestion or teaching that the PNAs of the invention can be used to enhance coagulation. Thus, there is no motivation to combine the PNAs described in *Shimkets* with the activator for plasma coagulation factor in *Kannemeier*.

Furthermore, the Office states that *Kannemeier* teaches that "FSAP and its proenzyme play a role in hemostasis and coagulation." Office Action at 11. However, *Kannemeier* does not teach using FSAP or its proenzyme in a pharmaceutical

preparation, and thus there would be no reason to modify the teachings of this reference to use it as a pharmaceutical preparation with a PNA. The recent Federal Circuit case, *Winner v. Wang*, states that in order to find a motivation to modify a reference, there must be some deficiency or problem perceived with the prior art reference. 53 U.S.P.Q.2d 1580, 1587 (Fed. Cir. 2000) (stating "there was no apparent disadvantage to the dead-bolt mechanism of Johnson, and therefore the motivation to combine would not stem from the "nature of the problem" facing one of ordinary skill in the art, because no "problem" was perceived). Similarly, there is no motivation to combine *Kannemeier* with *Shimkets*, as *Kannemeier* does not disclose a pharmaceutical preparation, nor any problem with pharmaceutical preparations promoting coagulation generally.

The Office has failed to establish a *prima facie* case of obviousness for at least the reasons stated above. Applicants respectfully submit that claims 1-3 are not obvious and request that the rejection be withdrawn.

Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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